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Original Article

IgE-mediated allergy in elderly patients with asthma

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Abstract

The incidence of a positive family history with asthma and levels of serum IgE and IgE antibodies were examined in 136 patients with asthma in relation to age at onset of the disease. The frequency of subjects with a family history of asthma ranged from 37.9 to 75.0% in all groups classified by age at onset. The frequency of patients with a high serum IgE level (≥150 IU/mL) was higher (51.7–63.2%) in all groups than the frequency of patients with a low serum level (< 150 IU/mL). The mean level of serum IgE was significantly higher in patients with a family history than in those without a family history, in subjects between the ages of 50 and 59 years at onset (mean age 63.4 years; $P < 0.02$) and in those over the age of 60 years at onset (74.0 years; $P < 0.01$). The number of patients with a positive RAST score either to house dust mite (HDM), cockroach, and *Candida* tended to decrease as the age at onset increased. However, the frequency of positive RAST to HDM was higher in patients with a family history and who were over the age of 50 years at onset compared with those patients between the ages of 40 and 49 years at onset, although the frequency was significantly higher in patients with family history than in those without family history ($P < 0.02$). These results suggest that IgE-mediated allergic reactions are significant not only in those patients who are younger, but also in elderly patients with asthma.

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Introduction

Bronchial asthma is characterized by bronchial hyperreactivity to various stimuli in which an IgE-mediated allergic reaction is considered to be the major factor affecting the pathophysiology of the airways. The IgE-mediated allergic reaction, which is closely associated with the mechanism of onset of asthma, has been recognized to change qualitatively and quantitatively with age.[1–7] Previous studies have shown that bronchial reactivity to methacholine and histamine release from leukocytes show a tendency to decrease with age.[8] Thus, asthma in older patients tends to have different characteristics from that in younger patients.

There are two different views regarding the significance of IgE-antibodies in the pathogenesis of asthma. One is that asthma is clinically classified into two types, atopic and non-atopic, on the basis of the presence or absence of IgE-mediated reactions,[9] where atopic asthma is more often found in the younger population and non-atopic asthma is found in the older patients. In contrast, there is a second concept that asthma is almost always associated with some type of IgE-related reaction.[10,11]

In the present study, age-related changes in serum IgE levels and the frequency of detection of specific IgE antibodies against inhalant allergens were examined. The results were analyzed with regard to subjects' family history of asthma.

Methods

The subjects of the present study were 136 patients (73 females, 63 males; mean age 59.4 years, range 15–90

years). The mean age at onset was 45.7 years and the mean level of serum IgE was 412 IU/mL. Of 136 subjects, 35 (25.7%) had steroid-dependent intractable asthma (SDIA), which was estimated by the amount and the duration of the systemic steroid required. Patients with SDIA comprised 21 females and 14 males (mean age 62.1 years, range 39–79 years; mean age at onset 47.7 years; mean level of serum IgE 400 IU/mL). Subjects were divided into two groups according to their family history of asthma. Subjects were also classified into four groups according to age at onset: 0–39, 40–49, 50–59 and 60+ years. Three inhalant allergens, house dust mite (HDM), cockroach and *Candida albicans*, were estimated by radioallergosorbent test (RAST). The level of serum IgE was measured by a radioimmunosorbent test (RIST).

Statistical analysis was estimated by using the χ^2 test and Student's *t*-test. A P value of < 0.05 was regarded as significant.

RESULTS

Table 1 shows patient characteristics classified by age at onset of the disease. The mean patient age in the four groups ranged from 45.6 to 74.0 years. The mean level of serum IgE was high, ranging from 310 to 480 IU/mL. The frequency of subjects with a family history of asthma ranged from 37.9% in patients over the age of 60 years at onset to 75.0% in those patients who were under the age of 39 years at onset. Even in patients between the ages of 50 and 59 years at onset, 22 of 39 subjects (61.1%) had a family history of asthma (Fig. 1).

The frequency of patients with a high serum IgE level (≥150 IU/mL) was greater (51.7–63.2%) in all groups classified by age at onset compared with the frequency of subjects with a low serum level (< 150 IU/mL; Fig. 2) and in patients over the age of 50 years at onset, the frequency of those with a high serum IgE level was significantly higher in patients with a family history of asthma than in subjects without family history of asthma (in subjects between the ages of 50 and 59 years at onset, $P < 0.01$; in subjects over the age of 60 years at onset, $P < 0.05$; Fig. 3). In contrast, the frequency of patients with a low serum IgE level (< 150 IU/mL) ranged from 37.5 to 47.3% and the frequency increased as the age at onset increased (Fig. 2).

In patients over the age of 50 years at onset, a correlation between a family history of asthma and serum IgE levels was found: the mean level of serum IgE was

Table 1. Characteristics of patients with asthma studied

Age at onset (years)	No. subjects	Mean age (years)	Serum IgE* (IU/mL)
0–39	33	45.6	480 (21–1531)
40–49	38	56.4	405 (6–4057)
50–59	36	63.4	310 (16–1986)
60+*	29	74.0	327 (5–974)

*Data are mean serum IgE levels, with the range given in parentheses.

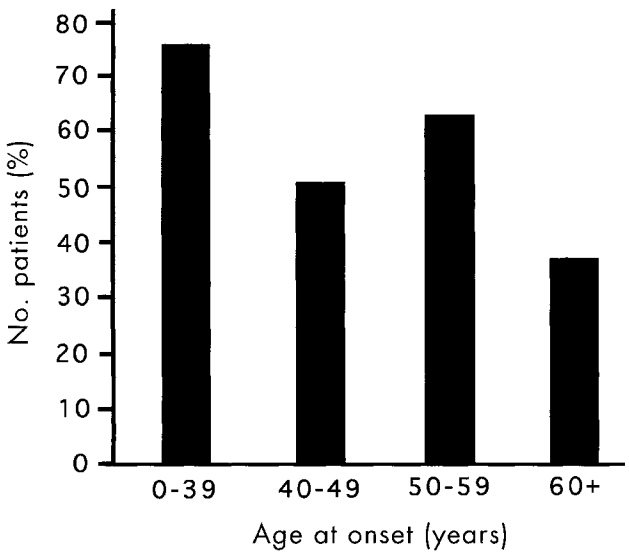

Fig. 1 Frequency of asthma patients with a family history of allergic disease and the age at onset.

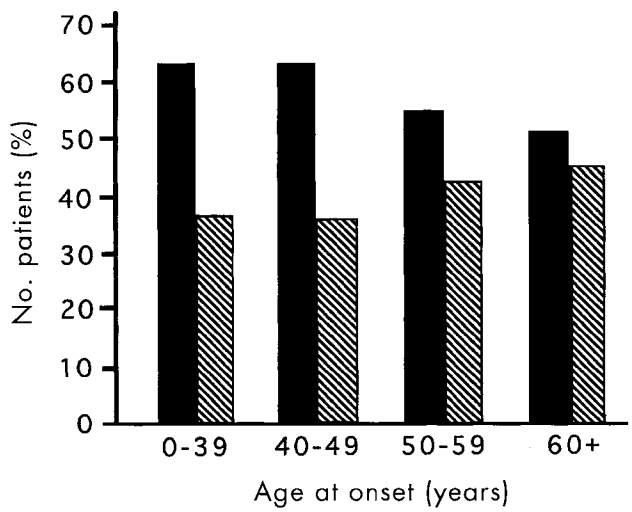

Fig. 2 Frequency of asthma patients with serum IgE levels either over 150 IU/mL (■) or less than 150 IU/mL (▨).

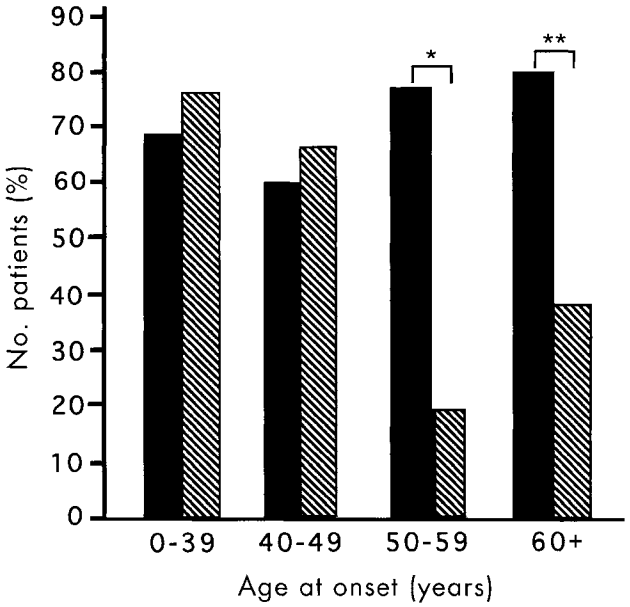

Fig. 3 Frequency of asthma patients with a serum IgE level over 150 IU/mL and a positive (■) or negative (▨) family history of allergic diseases.*$P < 0.01$, **$P < 0.05$.

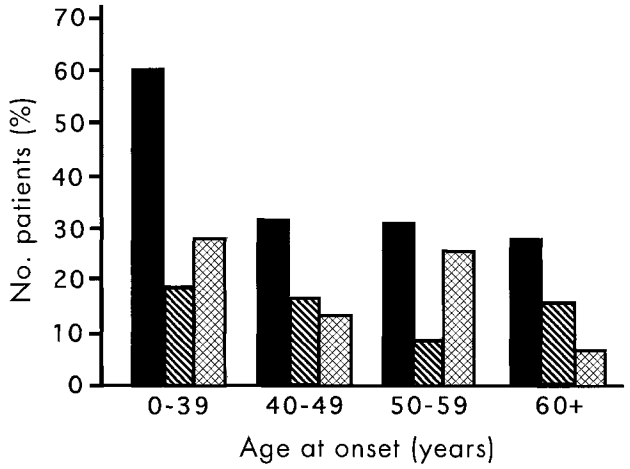

Fig. 4 Frequency of asthma patients with positive RAST to house dust mite (■), cockroach (▨) and *Candida* (▩) and the age at onset.

higher in patients with a family history of asthma than in subjects without family history and this difference was significant in patients between the ages of 50 and 59 years at onset ($P < 0.02$) and in those over the age of 60 years at onset ($P < 0.01$; Table 2).

Of the 136 subjects, a positive reaction in the RAST was observed in 51 (37.5%) for HDM, 20 (14.7%) for cockroach and 25 (18.4%) for *Candida albicans*. The frequency of patients with a positive RAST score to HDM tended to decrease as the age at onset increased.

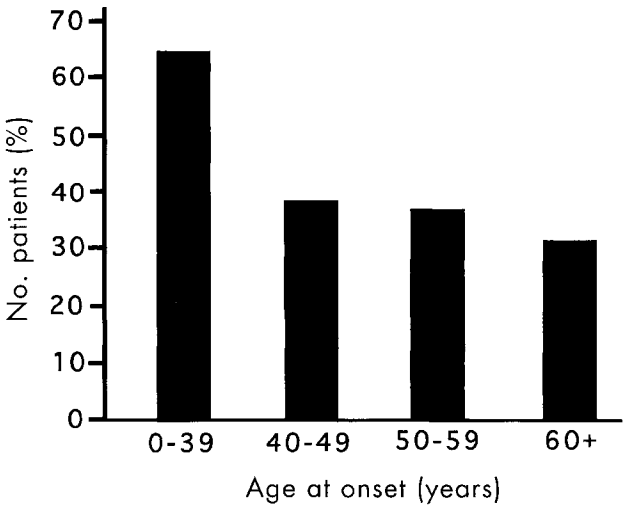

Fig. 5 Frequency of asthma patients with positive RAST either to house dust mite, cockroach or *Candida* and age at onset.

Table 2. Serum IgE levels in asthma patients with and without a family history of allergic disease

	Family history			
	(+)		(–)	
Age at onset (years)	No. subjects	Serum IgE† (IU/mL)	No. subjects	Serum IgE† (IU/mL)
0–39	25	508 (21–1531)	8	444 (44–1063)
40–49	20	522 (9–4057)	18	451 (6–3221)
50–59	22	434* (12–1987)	14	116* (63–250)
60+	11	548** (63–982)	18	191** (5–690)

†Data are the mean serum IgE level with the range given in parentheses. *$P < 0.02$, **$P < 0.01$.

However, even in patients over the age of 60 years at onset, 27.6% of subjects showed a positive reaction in the RAST to HDM. In contrast, the frequency of positive RAST to *Candida* was 25.0% in patients between the ages of 50 and 59 years at onset (Fig. 4). The positive RAST, either to HDM, cockroach or *Candida albicans*, showed a tendency to decrease as the age at onset increased (Fig. 5).

In patients over the age of 50 years at onset, the frequency of positive RAST to HDM was higher in patients with a family history of asthma than in subjects without family history and the difference was significant in patients over the age of 60 years at onset ($P < 0.02$; Fig. 6).

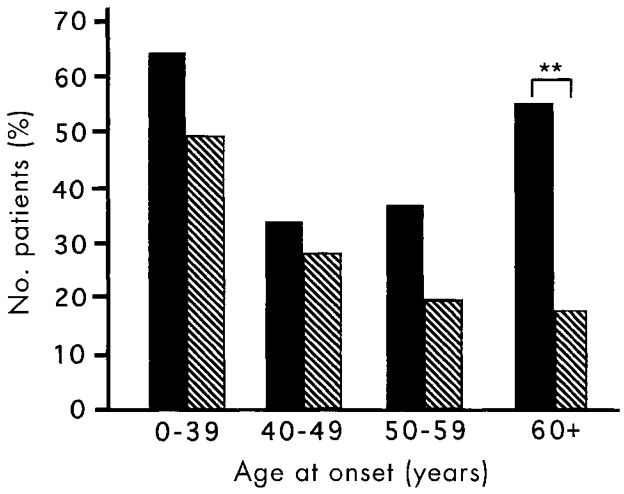

Fig. 6 Frequency of asthma patients with positive RAST to house dust mite and a positive (■) or negative (▨) family history of allergic diseases. *$P < 0.02$.

Discussion

In IgE-mediated allergic reactions associated with asthma, the release of chemical mediators, such as histamine and leukotrienes, occurs in the early stage of an asthma attack and inflammatory cell infiltration occurs in the airways at the late stage. In the inflammatory process, lymphocytes,[12,13] neutrophils,[14,15] eosinophils[16] and basophils[17] have been observed by analyzing the cellular composition of bronchoalveolar lavage (BAL) fluid.

These humoral and cellular factors in the onset of asthma may be affected by aging, which may alter the pathophysiology of asthma.[8,18-22] For example, for those under 30 years of age, a severe asthmatic attack can be induced by simple bronchoconstriction, while those between the ages of 31 and 40 years may be induced by bronchospasm and hypersecretion.[22,23] The frequency of patients with bronchospasm and hypersecretion shows a peak between the ages of 51 and 60 years, while the number of patients whose clinical findings show bronchiolar narrowing increases with age.[22] Furthermore, bronchial hyperresponsiveness shows a tendency to decrease in the elderly.[8]

Immunoglobulin E-mediated allergic reactions are also affected by aging.[5] Asthma is clinically divided into two types: atopic and non-atopic, in relation to the presence of IgE-mediated allergic reactions.[9] From this point of view, it has been suggested that many elderly asthmatics are non-atopic.

However, it should be noted that pathophysiology in the airways and IgE-mediated allergic reactions are basically different in elderly and in younger patients.

In the present study, the significance of an IgE-mediated allergic reaction in asthma in the elderly was estimated by observing serum IgE levels and IgE antibodies to inhalant allergens.

The frequency of patients with a family history of asthma was relatively high, even in patients between the ages of 50 and 59 years at onset (mean patient age 63.4 years; 61.1%) and in those over the age of 60 years at onset (mean patient age 74.0 years; 37.9%). The results suggest that many elderly asthmatics have an allergic constitution. The level of serum IgE and the frequency of positive RAST to HDM were higher in these patients with a family history of asthma than in those without a family history of asthma. The difference in serum IgE levels between patients with and without a family history of asthma was significant and the difference in positive RAST was also significant in patients over the age of 60 years at onset. These results demonstrate that many elderly asthmatics have a family history of asthma, which is closely related to serum IgE levels and positive RAST to HDM, indicating the significance of an IgE-mediated allergic reaction not only in the young but in elderly asthmatics as well.

References

1 Tanizaki Y, Komagoe H, Sudo M, Morinaga H, Kitani H, Kimura I. Comparison of basophil histamine release induced by the cross-linking of IgE receptors. *Acta Med. Okayama* 1985; **391**: 441–6.
2 Tanizaki Y, Komagoe H, Sudo M *et al.* Effect of aging on onset mechanism of bronchial asthma. 1. Immediate allergic reaction. *Jpn. J. Geriatr.* 1987; **23**: 317–21.
3 Tanizaki Y, Komagoe H, Sudo M *et al.* Effect of aging on onset mechanism of bronchial asthma. 2. Responsiveness of blood basophils. *Jpn. J. Geriatr.* 1987; **24**: 421–6.
4 Tanizaki Y, Sudo M, Kitani H *et al.* Clinical characteristics of bronchial asthma in the elderly in relation to cell components in the airways. *Jpn. J. Geriatr.* 1990; **27**: 589–94.
5 Tanizaki Y, Kitani H, Okazaki M, Mifune T, Mitsunobu F, Kimura I. Association of asthma with serum IgE and aging. Bronchoalveolar cells and the release of histamine and leukotrienes, LTC_4 and LTB_4, from leucocytes. *Jpn. J. Clin. Immunol.* 1993; **16**: 44–51.
6 Tanizaki Y, Kitani H, Okazaki M, Mifune T, Mitsunobu F, Kotoh N. Immunological responses to *Candida albicans* in patients with bronchial asthma and its relationship to patient age. *Jpn. J. Allergol.* 1992; **15**: 162–7.
7 Tanizaki Y, Kitani H, Okazaki M *et al.* Pathophysiological changes in the airways of asthma patients with aging. *Jpn. J. Allergol.* 1993; **41**: 1380–7.

8 Tanizaki Y, Kitani H, Okazaki M *et al.* Airway inflammation and bronchial hyperresponsiveness in patients with asthma. Comparison between atopic and nonatopic asthma. *Jpn. J. Allergol.* 1993; **42**: 26–33.
9 Ostergaard PA. Non-IgE mediated asthma in children. *Acta Paediatr. Scand.* 1985; **74**: 713–19.
10 Burrows B, Martinez FD, Halonen M, Barbee RA, Cline MG. Association of asthma with serum IgE levels and skin-test reactivity to allergens. *N. Engl. J. Med.* 1989; **320**: 271–7.
11 Tollerud DJ, O'Connor GT, Sparrow D, Weiss ST. Asthma, hay fever, and phlegm production associated with distinct patterns of allergy skin test reactivity, eosinophilia, and serum IgE levels. The normative aging study. *Am. Rev. Respir. Dis.* 1991; **144**: 776–81.
12 Walker C, Kaegi MK, Braun P, Blaser K. Activated T cells and eosinophilia in bronchoalveolar lavages from subjects with asthma correlated with disease severity. *J. Allergy Clin. Immunol.* 1991; **88**: 935–42.
13 Durham SSR, Ying S, Varney VA *et al.* Grass pollen immunotherapy inhibits allergen-induced infiltration of $CD4^+$, lymphocytes and eosinophils in the nasal mucosa and increases the number of cells expressing messenger RNA for interferon-γ . *J. Allergy Clin. Immunol.* 1996; **97**: 1356–65.
14 Hughes JM, McKay KO, Johnson PR, Tragoultas S, Black JL, Armour CL. Neutrophil-induced human bronchial hyperresponsiveness *in vitro*: Pharmacological modulation. *Clin. Exp. Allergy* 1993; **23**: 251–6.
15 Anticevich SZ, Hughes JM, Black JL, Armour CL. Induction of hyperresponsiveness in human airway tissue by neutrophils: Mechanism of action. *Clin. Exp. Allergy* 1993; **26**: 549–56.
16 Tanizaki Y, Kitani H, Okazaki M, Mifune T, Mitsunobu F, Kimura I. Mucus hypersecretion and eosinophils in bronchoalveolar lavage fluid in adult patients with bronchial asthma. *J. Asthma* 1993; **30**: 257–62.
17 Tanizaki Y, Kitani H, Okazaki M, Mifune T, Mitsunobu F, Kimura I. Changes in the proportions of bronchoalveolar lymphocytes, neutrophils and basophilic cells and the release of histamine and leukotrienes from broncho-alveolar cells in patients with steroid-dependent intractable asthma. *Int. Arch. Allergy Immunol.* 1993; **101**: 196–202.
18 Tanizaki Y, Komagoe H, Sudo M *et al.* Clinical studies on late onset asthma. 1. Anti-IgE induced release of histamine from whole blood. *Jpn. J. Allergol.* 1983; **32**: 1093–8.
19 Tanizaki Y, Komagoe H, Sudo M *et al.* Asthma classification based on clinical symptoms: Asthma type in relation to patient age and age at onset of disease. *Acta Med. Okayama* 1984; **38**: 471–6.
20 Tanizaki Y, Kitani H, Okazaki M *et al.* Cellular composition of fluid in the airways of patients with house dust sensitive asthma, classified by clinical symptoms. *Intern. Med.* 1992; **31**: 333–8.
21 Tanizaki Y, Kitani H, Okazaki M *et al.* Asthma classification by score calculated from clinical findings and examinations. *Jpn. J. Allergol.* 1992; **48**: 489–96.
22 Tanizaki Y, Kitani H, Okazaki M *et al.* A new modified classification of bronchial asthma based on clinical symptoms. *Intern. Med.* 1993; **32**: 197–203.
23 Tanizaki Y, Sudo M, Kitani H *et al.* Clinical studies on steroid-dependent intractable asthma. Comparison between early and late onset asthma. *Jpn. J. Allergol.* 1989; **38**: 68–73.